What is claimed is:

1. A method for detecting ββ-sheet conformation of insoluble proteins or prions in a sample comprising:
(a) reacting the sample with one or more α-helix or random coil conformational probes that interact with ββ-sheet conformation insoluble proteins or prions in the sample and thereby (i) undergo a conformational conversion to a predominately to ββ-sheet conformation, and (ii) form detectable aggregates with the β-sheet conformation insoluble proteins or prions in the sample; and
(b) detecting levels of detectable aggregates,
wherein levels of detectable aggregates correlate to the levels of ββ-sheet conformation insoluble proteins or prions in the sample.

2. A method of claim 1, wherein probe termini are bound to moieties that are optically detectable when the probes form detectable aggregates with the ββ-sheet conformation insoluble proteins or prions in the sample.

3. A method of claim 2, wherein the moieties are fluorophores.

4. A method of claim 1, wherein probe termini are bound to radionucleotide moieties that are detectable when the probes form detectable aggregates with the ββ-sheet conformation insoluble proteins or prions in the sample.

5. A method of claim 1, wherein the probes comprise at least two amino acid sequences that are complimentary to amino acid sequences of the ββ-sheet conformation insoluble proteins or prions.

6. A method of claim 1, wherein one or more of the probes comprise at least two amino acid sequences that are homologous to amino acid sequences of the ββ-sheet conformation insoluble proteins or prions.

7. A method claim 6, wherein one or more of the probes is a palindromic probe.

8. A method of claim 1, wherein the ββ-sheet conformation insoluble proteins or prions are selected from the group consisting of low-density lipoprotein receptor, cystic fibrosis transmembrane regulator, Huntingtin, Abeta peptide, prions, insulin-related amyloid, hemoglobin, alpha synuclein, rhodopsin, crystallins, and p53.

9. A method of claim 1, where one or more probes is a palindromic 33_mer comprising amino acid sequences that are homologous to amino acids 122-104 and 109-122 of the $PrP^{SC}$ protein (SEQ ID NO: 1 or 29).*33_mer palindrome*

**VVAGAAAAGAVHKLNTKPKLKHVAGAAAAGAVV (murine)**

**VVAGAAAAGAMHKMNTKPKMKHMAGAAAAGAVV (human)**

10. A method of claim 1, wherein one or more probes is a palindromic 33_mer comprising amino acid sequences that are equivalent to amino acids 122-104 and 109-122 of the $PrP^{SC}$ protein (SEQ ID NO: 1 or 29).*33_mer palindrome*

**VVAGAAAAGAVHKLNTKPKLKHVAGAAAAGAVV (murine)**

**VVAGAAAAGAMHKMNTKPKMKHMAGAAAAGAVV (human)**

11. A method of claim 1, wherein one or more probes is a palindromic 33_mer comprising amino acid sequences that are between about 70% to about 90% identical to amino acids 122-104 and 109-122 of the $PrP^{SC}$ protein (SEQ ID NO:1 or 29).*33_mer palindrome*

**VVAGAAAAGAVHKLNTKPKLKHVAGAAAAGAVV (murine)**

**VVAGAAAAGAMHKMNTKPKMKHMAGAAAAGAVV (human)**

12. A method of claim 1, wherein one or more probes is a probe comprising amino acid sequences that are homologous to amino acids 1-40 of the Abeta peptide Nref 00111747 (human)

DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVV SEQ ID NO: 4 .

13. A method of claim 1, wherein one or more probes comprise amino acid sequences that are equivalent to amino acids 1-40 of the Abeta peptide (SEQ ID NO:4). DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVV.

14. A method of claim 1, wherein one or more probes comprise amino acid sequences that are between about 70% to about 90% identical to amino acids 1-40 of the A.beta peptide (SEQ ID NO:4)

DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVV.

15. A method of claim 1, wherein one or more probes comprise an amino acid sequence that has a helix-loop-helix conformation found in polylysine and that is equivalent to SEQ ID NO: 8. KKKKKKKKKKKKKKKKKKKKKKKKKK.

16. A method of claim 1, wherein one or more probes comprise an amino acid sequence that has a helix-loop-helix conformation found in polylysine and that is homologous to SEQ ID NO: 8. KKKKKKKKKKKKKKKKKKKKKKKKKKKKKK.

17. A method of claim 1, wherein one or more probes comprise an amino acid sequence that has a helix-loop-helix conformation found in polylysine and that is equivalent to SEQ ID NO: 8 KKKKKKKKKKKKKKKKKKKKKKKKKKKKKK .

18. A method of claim 1, wherein one or more probes comprise an amino acid sequence that has a helix-loop-helix conformation found in polylysine and that is between about 70% to about 90% identical to SEQ ID NO: 8. KKKKKKKKKKKKKKKKKKKKKKKKKKKKKK .

19. A method of claim 1, wherein one or more probes comprise amino acid sequences that are homologous to amino acids 104-122 of wild-type (wt) TSE (SEQ ID NO:10) **KPKTNLKHVAGAAAAGAVV**.

20. A method of claim 1, wherein one or more probes comprise amino acid sequences that are equivalent to amino acids 104-122of wild-type (wt) TSE (SEQ ID NO:10). **KPKTNLKHVAGAAAAGAVV**

21. A method of claim 1, wherein one or more probes comprise amino acid sequences that are between about 70% to about 90% identical to amino acids 104-122 of wild-type (wt) TSE (SEQ ID NO:10) **KPKTNLKHVAGAAAAGAVV.**

22. A method of claim 1, wherein one or more probes comprise an amino acid sequence that: (a) is a selectively mutated TSE sequence; and (b) is destabilized and noninfectious; and (c) has an amino acid sequence that is homologous to SEQ ID NO: 10 **KPKTNLKHVAGAAAAGAVV.**

23. A method of claim 1, wherein one or more probes comprise an amino acid sequence that: (a) is a selectively mutated TSE sequence; (b) is destabilized and noninfectious; and (c) has an amino acid sequence that is equivalent to SEQ ID NO: 10 **KPKTNLKHVAGAAAAGAVV.**

24. A method of claim 1, wherein one or more probes comprise an amino acid sequence that: (a) is a selectively mutated TSE sequence; (b) is destabilized and noninfectious; and (c) has an amino acid sequence that is between about 70% to about 90% identical to SEQ ID NO: 10 **KPKTNLKHVAGAAAAGAVV.**

25. The method of claim 1, wherein the probes comprise an extrinsic fluor.

26. The method of claim 25, wherein the extrinsic fluor is pyrene.

27. A method of claim 1, further comprising reacting the sample and probes prior to detecting with a probe that limits the formation of detectable aggregates to detectable but non-infectious levels.

28. A method of claim 1, wherein levels of detectable aggregates are compared to levels of ββ-sheet conformation insoluble proteins or prions associated with amyloidogenic diseases.

29. A method of claim 1, wherein the ββ-sheet conformation insoluble proteins or prions form amyloid plaques or amyloid deposits associated with amyloidogenic diseases.

30. A method of claim 1, wherein the sample is disaggregated prior to reaction with the probe.

31. A method of claim 1, wherein the sample is a tissue sample or is a liquid biological material obtained from spinal fluid, saliva, urine or other bodily fluids.

32. A method of claim 1, wherein excimers are formed by reacting one or more α-helix or random coil conformational probes with ββ-sheet conformation insoluble proteins or prions in the sample.

33. A kit comprising one or more α-helix or random coil conformational probes that interact with β-sheet conformation insoluble proteins or prions in a sample and thereby (a) undergo a conformational conversion to a predominately to ββ-sheet conformation, and (b) form detectable aggregates with the ββ-sheet conformation insoluble proteins or prions in the sample,
wherein levels of detectable aggregates correlate to the levels of ββ-sheet conformation insoluble proteins or prions in the sample.

34. A kit of claim 33, wherein probe termini are bound to moieties that are optically detectable when the probes form detectable aggregates with ββ-sheet conformation insoluble proteins or prions in a sample.

35. A kit of claim 34, wherein the moieties are fluorophores.

36. A kit of claim 33, wherein probe termini are bound to radionuclide moieties that are detectable when the probes form detectable aggregates with ββ-sheet conformation insoluble proteins or prions in a sample.

37. A kit of claim 33, wherein the probes comprise at least two amino acid sequences that are complementary to amino acid sequences of ββ-sheet conformation insoluble proteins or prions.

38. A kit of claim 33, wherein one or more of the probes comprise at least two amino acid sequences that are homologous to amino acid sequences of ββ-sheet conformation insoluble proteins or prions.

39. A kit of claim 33, wherein one or more of the probes comprise an amino acid sequence of SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 15, 18, 20, 22, 23, 24, 25 or 27.

40. A kit of claim 33, wherein the ββ-sheet conformation insoluble proteins or prions are selected from the group consisting of low-density lipoprotein receptor, cystic fibrosis transmembrane regulator, Huntingtin, Abeta peptide, prions, insulin-related amyloid, hemoglobin, alpha synuclein, rhodopsin, crystallins, and p53.

41. A kit of claim 33, where one or more probes is a palindromic 33_mer comprising amino acid sequences that are homologous to amino acids 122-104 and 109-122 of the human or murine $PrP^{SC}$ protein (SEQ ID NO: 1 or 29)

**VVAGAAAAGAVHKLNTKPKLKHVAGAAAAGAVV (murine)**

**VVAGAAAAGAMHKMNTKPKMKHMAGAAAAGAVV (human)**

42. A kit of claim 33, wherein one or more probes is a palindromic 33_mer comprising amino acid sequences that are equivalent to amino acids 122-104 and 109-122 of the $PrP^{SC}$ protein (SEQ ID NO: 1 or 29).

**VVAGAAAAGAVHKLNTKPKLKHVAGAAAAGAVV (murine)**

**VVAGAAAAGAMHKMNTKPKMKHMAGAAAAGAVV (human)**

43. A kit of claim 33, wherein one or more probes is a palindromic 33_mer comprising amino acid sequences that are between about 70% to about 90% identical to amino acids 122-104 and 109-122 of the $PrP^{SC}$ protein (SEQ ID NO: 1 or 29).

**VVAGAAAAGAVHKLNTKPKLKHVAGAAAAGAVV (murine)**

**VVAGAAAAGAMHKMNTKPKMKHMAGAAAAGAVV (human)**

44. A kit of claim 33, wherein one or more probes is a probe comprising amino acid sequences that are homologous to amino acids 1-40 of the Abeta peptide (SEQ ID NO: 4). DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVV

45. A method of claim 1, wherein one or more probes comprise amino acid sequences that are equivalent to amino acids 1-40 of the Abeta peptide (SEQ ID NO:4). DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVV.

46. A kit of claim 33, wherein one or more probes comprise amino acid sequences that are between about 70% to about 90% identical to amino acids 1-40 of the Abeta peptide (SEQ ID NO:4). DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVV.

47. A kit of claim 33, wherein one or more probes comprise an amino acid sequence that is equivalent or homologous to SEQ ID NO: 9 or 20.

48. A kit of claim 33, wherein one or more probes comprise an amino acid sequence that has a helix-loop-helix conformation found in polylysine and that is homologous to SEQ ID NO: 8.

49. A kit of claim 33, wherein one or more comprise an amino acid sequence that has a helix-loop-helix conformation found in polylysine and that is equivalent to SEQ ID NO: 8_.

50. A kit of claim 33, wherein one or more probes comprise an amino acid sequence that has a helix-loop-helix conformation found in polylysine and that is between about 70% to about 90% identical to SEQ ID NO: 9.

51. A kit of claim 33, wherein one or more probes comprise amino acid sequences that are homologous to amino acid sequences 104-122 of wild-type (wt) TSE (SEQ ID NO:10). **KPKTNVKHVAGAAAAGAVV**

52. A kit of claim 33, wherein one or more probes comprise amino acid sequences that are equivalent to amino acid sequences 104-122 of wild-type (wt) TSE (SEQ ID NO:10). **KPKTNVKHVAGAAAAGAVV**

53. A kit of claim 33, wherein one or more probes comprise amino acid sequences that are between about 70% to about 90% identical to amino acid sequences 104-122 of wild-type (wt) TSE (SEQ ID NO:10). **KPKTNVKHVAGAAAAGAVV**

54. A kit of claim 33, wherein one or more probes comprise an amino acid sequence that: (a) is a selectively mutated TSE sequence; (b) is destabilized and noninfectious; and (c) has an amino acid sequence that is homologous to SEQ ID NO:10.

55. A kit of claim 33, wherein one or more probes comprise an amino acid sequence that: (a) is a selectively mutated TSE sequence; (b) is destabilized and noninfectious; and (c) has an amino acid sequence that is equivalent to SEQ ID NO: 10.

56. A kit of claim 33, wherein one or more probes comprise an amino acid sequence that: (a) is a selectively mutated TSE sequence; (b) is destabilized and noninfectious; and (c) has an amino acid sequence that is between about 70% to about 90% identical to SEQ ID NO: 10.

57. A kit of claim 33, wherein the probes comprise an extrinsic fluor.

58. A kit of claim 57, wherein the extrinsic flour is pyrene.

59. A kit of claim 33, further comprising a pendant probe that limits the formation of detectable aggregates to detectable but non-infectious levels.

60. A method of diagnosing whether a subject suffers from, or is predisposed to, a disease associated with conformationally altered proteins or prion comprising:
(a) obtaining a sample from the subject;
(b) reacting the sample with one or more α-helix or random coil conformational probes that interact with ββ-sheet conformation insoluble proteins or prions in the sample and thereby (i) undergo a conformational conversion to a predominately to ββ-sheet conformation, and (ii) form detectable aggregates with the ββ-sheet conformation insoluble proteins or prions in the sample; and
(c) detecting levels of detectable aggregates,
wherein levels of detectable aggregates correlate to the amount of ββ-sheet conformation insoluble proteins or prions in, and level of infectiousness of, the sample and indicate whether the subject suffers from, or is predisposed to, a disease associated with ββ-sheet conformation insoluble proteins or prions.

61. A method of claim 60, wherein probe termini are bound to moieties that are optically detectable when the probes form detectable aggregates with the ββ-sheet conformation insoluble proteins or prions in the sample.

62. A method of claim 61, wherein the moieties are fluorophores.
63. A method of claim 60, wherein probe termini are bound to radionuclide moieties that are detectable when the probes form detectable aggregates with the ββ-sheet conformation insoluble proteins or prions in the sample.

64. A method of claim 60, wherein the probes comprise at least two amino acid sequences that are complimentary to amino acid sequences of the ββ-sheet conformation insoluble proteins or prions.

65. A method of claim 60, wherein one or more of the probes comprise at least two amino acid sequences that are homologous to amino acid sequences of the ββ-sheet conformation insoluble proteins or prions.

66. A method claim 60, wherein one or more of the probes comprise an amino acid sequence of SEQ ID NO: 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11, 12, 15, 18, 20, 22, 23, 24, 25 or 27.

67. A method of claim 60, wherein the ββ-sheet conformation insoluble proteins or prions are selected from the group consisting of low-density lipoprotein receptor, cystic fibrosis transmembrane regulator, Huntingtin, Abeta peptide, prions, insulin-related amyloid, hemoglobin, alpha synuclein, rhodopsin, crystallins, transthyretin, gelsolin, cystatins and p53.

68. A method of claim 60, where one or more probes is a palindromic 33_mer comprising amino acid sequences that are homologous to amino acids 122-104 and 109-122 of the $PrP^{SC}$ protein (SEQ ID NO: 1 or 29).

**VVAGAAAAGAVHKLNTKPKLKHVAGAAAAGAVV (murine)**

**VVAGAAAAGAMHKMNTKPKMKHMAGAAAAGAVV (human)**

69. A method of claim 60, wherein one or more probes is a palindromic 33_mer comprising amino acid sequences that are equivalent to amino acids 122-104 and 109-122 of the $PrP^{SC}$ protein (SEQ ID NO:1 or 29)

**VVAGAAAAGAVHKLNTKPKLKHVAGAAAAGAVV (murine)**

**VVAGAAAAGAMHKMNTKPKMKHMAGAAAAGAVV (human)**

70. A method of claim 60, wherein one or more probes is a palindromic 33_mer comprising amino acid sequences that are between about 70% to about 90% identical to amino acids 122-104 and 109-122 of the $PrP^{SC}$ protein (SEQ ID NO: 1 or 29).

**VVAGAAAAGAVHKLNTKPKLKHVAGAAAAGAVV (murine)**

**VVAGAAAAGAMHKMNTKPKMKHMAGAAAAGAVV (human)**

71. A method of claim 60, wherein one or more probes is a probe comprising amino acid sequences that are homologous to amino acids 1-40 of the Abeta peptide (SEQ ID NO:4) DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVV.

72. A method of claim 60, wherein one or more probes comprise amino acid sequences that are equivalent to amino acids 1-40 of the Abeta peptide (SEQ ID NO:4) DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVV

73. A method of claim 60, wherein one or more probes comprise amino acid sequences that are between about 70% to about 90% identical to amino acids 1-40 of the Abeta peptide (SEQ ID NO:4). DAEFRHDSGYEVHHQKLVFFAEDVGSNKGAIIGLMVGGVV

74. A method of claim 60, wherein one or more probes comprise an amino acid sequence that is an oligo or polylysine.

75. A method of claim 74, wherein said probe is homologous to SEQ ID NO: 8.

76. A method of claim 60, wherein said probe is equivalent to SEQ ID NO: 8.

77. A method of claim 60, wherein one or more probes comprise an amino acid sequence that has a helix-loop-helix conformation found in lysine and that is between about 70% to about 90% identical to oligo- or polylysine.

78. A method of claim 61, wherein one or more probes comprise amino acid sequences that are homologous or equivalent to amino acids 104-122 of wild-type (wt) TSE (SEQ ID NO:10).

79. A method of claim 60, wherein one or more probes comprise an amino acid sequence that: (a) is a selectively mutated TSE sequence; (b) is destabilized and noninfectious; and (c) has an amino acid sequence that is homologous or equivalent to SEQ ID NO: 10.

80. A method of claim 61, wherein one or more probes comprise an amino acid sequence that: (a) is a selectively mutated TSE sequence; (b) is destabilized and noninfectious; and (c) has an amino acid sequence that is between about 70% to about 90% identical to SEQ ID NO: 10.

81. A method of claim 60, wherein the probes comprise an extrinsic fluor.

82. The method of claim 60, wherein the extrinsic flour is pyrene.

83. A method of claim 60, further comprising reacting the sample and probes prior to detecting with a pendant probe that limits the formation of detectable aggregates to detectable but non-infectious levels.

84. A method of claim 60, wherein levels of detectable aggregates are compared to levels of ββ-sheet conformation insoluble proteins or prions associated with amyloidogenic diseases.

85. A method of claim 60, wherein the ββ-sheet conformation insoluble proteins or prions form amyloid plaques or amyloid deposits associated with amyloidogenic diseases.

86. A method of claim 60, wherein the sample is disaggregated prior to reaction with the probe.

87. A method of claim 60, wherein the sample is a tissue sample or is a liquid biological material obtained from spinal fluid, saliva, urine or other bodily fluids.

88. A method of claim 60, wherein exi_mers are formed by reacting one or more α-helix or random coil conformational probes with ββ-sheet conformation insoluble proteins or prions in the sample.

89. A palindromic peptide probe comprising three peptide sections, a first peptide section, a second peptide section and a third peptide section, said first and said third sections comprising peptide sequences each of which comprises at least 5 amino acids identical to a peptide fragment from a target insoluble protein which is responsible for ββ-sheet formation in said target insoluble protein and wherein at least a portion of said first peptide section is a palindrome of at least a portion of said third peptide section, said first peptide section or said third peptide section being identical to at least a five amino acid peptide sequence in said peptide fragment from said target insoluble protein, said second peptide sequence comprising between 1 and 10 amino acid units one of which is a proline residue.

90. The probe according to claim 89 wherein said first and said third sections are endcapped with hydrophobic amino acids which can be chemically modified or complexed to accommodate a chemical moiety capable of being measured.

91. The probe according to claim 90 wherein said chemical moiety is a chromophore and both said first and third peptide sections of said probe comprise said chromophore.

92. The probe according to claim 90 wherein said chromophore is selected from the group consisting of pyrene, tryoptophan, flureseeing rhodamine.

93. The probe according to claim 92 which is in the form of an excimer.

94. The probe according to claim 89 wherein said second proline section comprises between 1 and 5 amino acid residues all of which are proline residues.

95. The probe according to claim 89 wherein said target peptide is selected from the group consisting of low-density lipoprotein receptor, cystic fibrosis transmembrane regulator, Huntingtin, Abeta peptide, prions, insulin-related amyloid, hemoglobin, alpha synuclein, rhodopsin, crystallins, transthyretin, gelsolin, cystatins and p53.

96. The probe according to claim 89 wherein said first peptide section and said third peptide section consist of identical amino acids.

97. The probe according to claim 89 wherein said first and said second peptide sections each comprise about 10 to about 25 amino acid residues.

98. The palindromic probe according to claim 89 selected from the group consisting of SEQ ID NO: 1, 18, 23, 25, 27 and 29.

99. The method according to claim 60 wherein said disease is Alzheimer's Disease, Prion diseases, Creutzfeld Jakob disease, scrapie and bovine spongiform encephalopathy ($PrP^{Sc}$ ); ALS (SOD and neurofilament); Pick's disease ; Parkinson's disease, Frontotemporal dementia; Diabetes Type II (Amylin); Multiple myeloma-- plasma cell dyscrasias; Familial amyloidotic polyneuropathy; Medullary carcinoma of thyroid; Chronic renal failure, Congestive heart failure, Senile cardiac and systemic amyloidosis (Transthyretin), Chronic inflammation, Atherosclerosis, Familial amyloidosis, or Huntington's disease.